

Please delete the Title of the Invention and insert therefor -- SEQUENCES ENCODING NOVEL HUMAN THYROID PEROXIDASE PROTEINS AND POLYPEPTIDES --.

REMARKS

The Restriction Requirement

Applicant notes that the Examiner has made the Restriction Requirement final. The Examiner's decision is regretted since, as noted by Applicant in its Response and as acknowledged by the Examiner, the claims of the instant divisional application correspond to Group IV of the four-way Restriction Requirement issued in the parent application. With respect, the Examiner's assertion in Paper No. 8 that "the restriction requirement of the instant application is not identical to that of the parent application" was and is in error. As argued in Applicant's Response, the claims of the instant divisional application correspond to Group IV, elected by applicant previously in response to the Restriction Requirement issued in the parent application, since claim 37 is, in fact, identical in its broadest scope to the corresponding and cancelled claim 28 depending from cancelled claim 25.

Accordingly, as argued by Applicant in its response, § 1.129(b) is not available. Further, given the identity, in their broadest scope, of claims 37 and 28, there is no logical or technical basis for requiring restriction of claims designated in the parent application as falling within a single Examiner-identified Group. In view of these

remarks, reconsideration is again requested, particularly since, given that all the claims in Group IV share Class and Subclass designations, search and examination of the entire Group can be made without serious burden, MPEP § 803, and Applicant otherwise respectfully reserves its right to petition the Commissioner to review the requirement. MPEP § 1.144.

The Declaration

The Examiner has objected that the declaration is defective because it omits the post office address of the inventor, Dr. Rapoport. The Examiner has also required correction of the priority claim to PCT/US92/0731 and PCT/US92/06283.

Applicant submits herewith a new Declaration of the inventor, Dr. Rapoport, which is believed to satisfy the Examiner's objections. The Examiner is thanked for bringing this to Applicant's attention.

Informalities in the Specification

The Examiner has objected to the Brief Description of the Drawings as informal for failing to refer to figure panels and for not appearing on consecutive pages within the specification, and has required correction. The Applicant notes the Examiner's objections with appreciation. The Examiner is respectfully requested to hold these objections in abeyance pending notification of allowable subject matter, at which time an appropriate amendment addressing these objections will be prepared and filed.

Similarly, it is respectfully requested that Examiner hold in abeyance the objections to informalities in the figures pending notification of allowable subject matter, at which time formal drawings will be submitted.

The Examiner has objected to the Abstract of the Disclosure and to the Title of the Invention as not descriptive of the invention as currently claimed. By amendment submitted herewith, entry of which is respectfully requested, Applicant has amended the Abstract and Title as required by the Examiner. No issue of new matter should arise, and the Examiner is thanked for her suggestion to improve the clarity of the specification.

The Rejections Under § 112 May Properly Be Withdrawn

The Examiner has objected to the specification under 35 U.S.C. § 112, first paragraph, as failing to provide sufficient guidance to enable one skilled in the art to make/use a recombinant DNA sequence encoding human thyroid peroxidase which is secreted from a host cell. The Examiner further asserts that the disclosure appears to be enabling and descriptive only for claims limited to the secretable human thyroid peroxidase in which stop codons are present at nucleotide positions 2629-31 and 2641-43 and its production by CHO cells. Further, the Examiner asserts that the specification does not enable the skilled person to make and/or use the invention commensurate in scope with the claims, noting that the claims as written read on any possible cell, and that the specification gives no guidance on or exemplification of the

production and secretion of thyroid peroxidase by any host cell other than CHO cells. These objections and grounds of rejection are respectfully traversed.

Contrary to the Examiner's assertions, it is respectfully submitted that the person of ordinary skill who reads and understands the teachings of the specification, including the numerous examples and screening methods described, would be fully capable of carrying out the invention as presently claimed without undue experimentation, and with the exercise of no more than ordinary skill. It will be appreciated that, by following the teachings of the specification, including the methods taught for screening suitable secretable human thyroid peroxidase proteins and peptides, DNA sequences useful according to the invention may be selected for testing and evaluation in the ordinary course of laboratory efforts in the pertinent field.

It will further be appreciated that Dr. Rapoport, the inventor of the instant application, was the first to describe truncated, secretable forms of human thyroid peroxidase, which have since become important tools in human clinical immunodiagnostics. His pioneering work is entitled to a broad scope of protection commensurate with the fact that he has described and enabled the production and practical application of secretable human thyroid peroxidase and the expression thereof using the appropriate sequences selected according to the teachings of the invention.

Similarly, the Examiner's assertion that cell types other than mammalian CHO cells are not disclosed is incorrect and, in any event, the issue of selection of

appropriate signals for nucleic acid translation and transcription, codon usage, and the like noted by Examiner are, in light of Dr. Rapoport's contributions, capable of being addressed and resolved in the normal course by persons of ordinary skill who appreciate and understand the present invention, without undue experimentation. Indeed, the Examiner has pointed to no issue of enablement which will not admit of resolution by the ordinary skilled artisan in light of the specification. Accordingly, withdrawal of the rejections is deemed appropriate, and is respectfully requested.

The Examiner has objected to the claims under 35 U.S.C. § 112, second paragraph, as indefinite in the recitation of "human thyroid peroxidase," asserting that it fails to set forth the essential characteristics and aspects Applicant intends to claim. The Examiner also objects to the phrase "recombinant DNA sequences encoding human thyroid peroxidase which is secreted from a cell" and to the phrase "a stop codon upstream" as failing to set forth exactly how far upstream Applicant intends said stop codon to lie. These grounds of rejection are respectfully traversed.

It is respectfully submitted that the person of ordinary skill who reads and understands the specification of the instant application will fully appreciate the meaning and scope of "human thyroid peroxidase" as set forth therein. The "essential characteristic" of human thyroid peroxidase, for the purpose of claims 11-15, is that it is capable of being "secreted from a cell," as recited therein. Other than that, the term "human thyroid peroxidase" may have any or all of the characteristics and aspects known by those of skill and described in the specification (the entire specification is directed to it), and it is respectfully submitted that its use in the claims comports

with 35 U.S.C. § 112, second paragraph. It is further respectfully urged that the meaning of "recombinant DNA sequences encoding human thyroid peroxidase which is secreted from a cell" is definite and will be understood by the person of ordinary skill who reads the specification, and who will appreciate that it is the human thyroid peroxidase which is secreted from a cell. With respect to the recitation of the phrase "a stop codon upstream," it is respectfully submitted that the meaning of this also will be evident to the person of ordinary skill, who will appreciate that a recited upstream stop codon, for the purposes of the claims, is one that will function as a stop codon. As this will be appreciated by the person of ordinary skill, it is not necessary to set forth in the claim "exactly how far upstream" the stop codon is found to satisfy the requirements of 35 U.S.C. § 112, second paragraph. Accordingly, withdrawal of the rejections is believed proper, and is respectfully requested.

The Rejection Under § 101 May Properly Be Withdrawn

The Examiner has rejected claims 11-13 under 35 U.S.C. § 101, as directed to non-statutory subject matter. Specifically, the Examiner asserts that the recombinant DNA sequence reads on DNA as it exists in nature. This ground of rejection is respectfully traversed. According to Walker & Cox, The Language of Biotechnology, American Chemical Society, Publisher (1988), "recombinant DNA" is defined as "a DNA molecule formed in vitro by ligating DNA molecules that are not normally joined." It is respectfully urged that recombinant DNA does not exist in nature.

Accordingly, it is believed that this ground of rejection may be properly withdrawn, and the same is respectfully requested.

The Rejection Under § 103 May Properly Be Withdrawn

The Examiner has rejected Claims 11-15 under 35 U.S.C. § 103 as unpatentable over Seto et al. or Libert et al. in view of Lee et al. or Sellis et al. or Rose et al. and Magnusson et al. This ground of rejection is respectfully traversed.

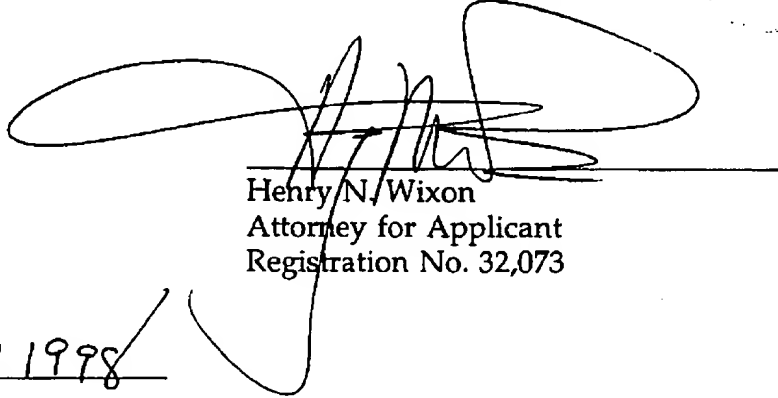
The Examiner admits that neither of the primary references teaches a recombinant DNA sequence encoding human thyroid peroxidase which is secreted from a cell with stop codons upstream from a transmembrane domain, a vector which comprises the DNA sequence or a host cell transformed with the vector.

Accepting, *arguendo*, the Examiner's characterization of the primary and secondary references, it is respectfully urged that none of the secondary references satisfies the failings of the primary references, and that none of the references, alone or in any combination, provides the suggestion to combine required to state a proper *prima facie* obviousness rejection of Dr. Rapoport's invention, described and claimed in the present application. In fact, it is respectfully urged that the Examiner has necessarily and improperly looked to the specification of the instant application, in hindsight, to supply to the missing suggestion to combine which the Examiner has not found in any of the primary or secondary references. It is further respectfully submitted that the Examiner has failed to state a *prima facie* case of obviousness and

that the rejection must fail. Accordingly, withdrawal of the rejection is believed appropriate, and is respectfully requested.

In view of the preceding remarks, it is believed that the application is in condition for immediate allowance, and early notice to this effect is respectfully requested.

Respectfully submitted,

A large, stylized handwritten signature in black ink, consisting of several loops and a long horizontal stroke, positioned above the printed name and title.

Henry N. Wixon
Attorney for Applicant
Registration No. 32,073

Dated: 21 JULY 1998
Hale and Dorr LLP
1455 Pennsylvania Avenue, N.W.
Washington, D.C. 20004
(202) 942-8459/Telephone
(202) 942-8484/Facsimile